SUPPLEMENTARY MATERIAL

Marine Natural Products as Acetylcholinesterase Inhibitor: Comparative Quantum Mechanics and Molecular Docking Study

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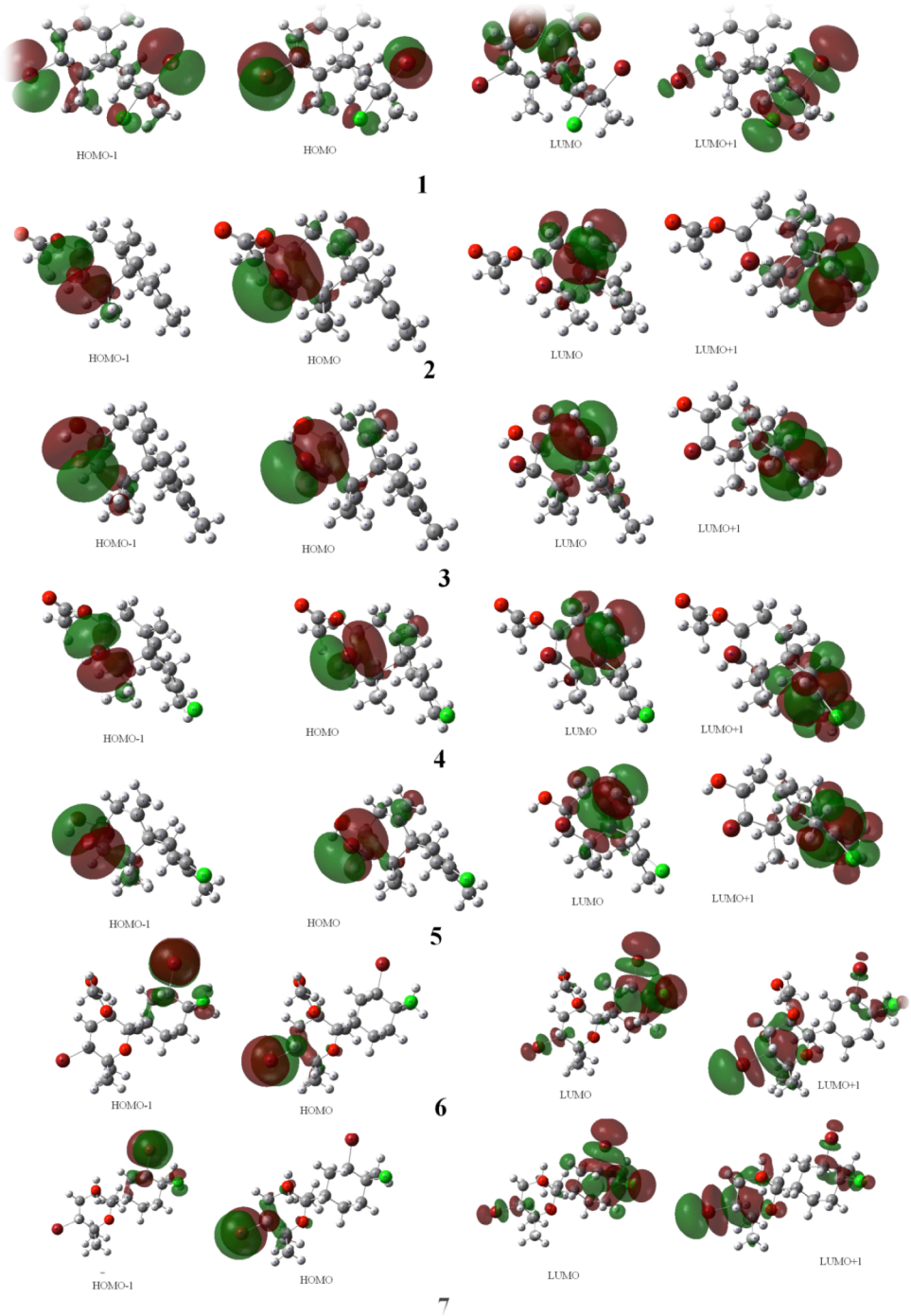
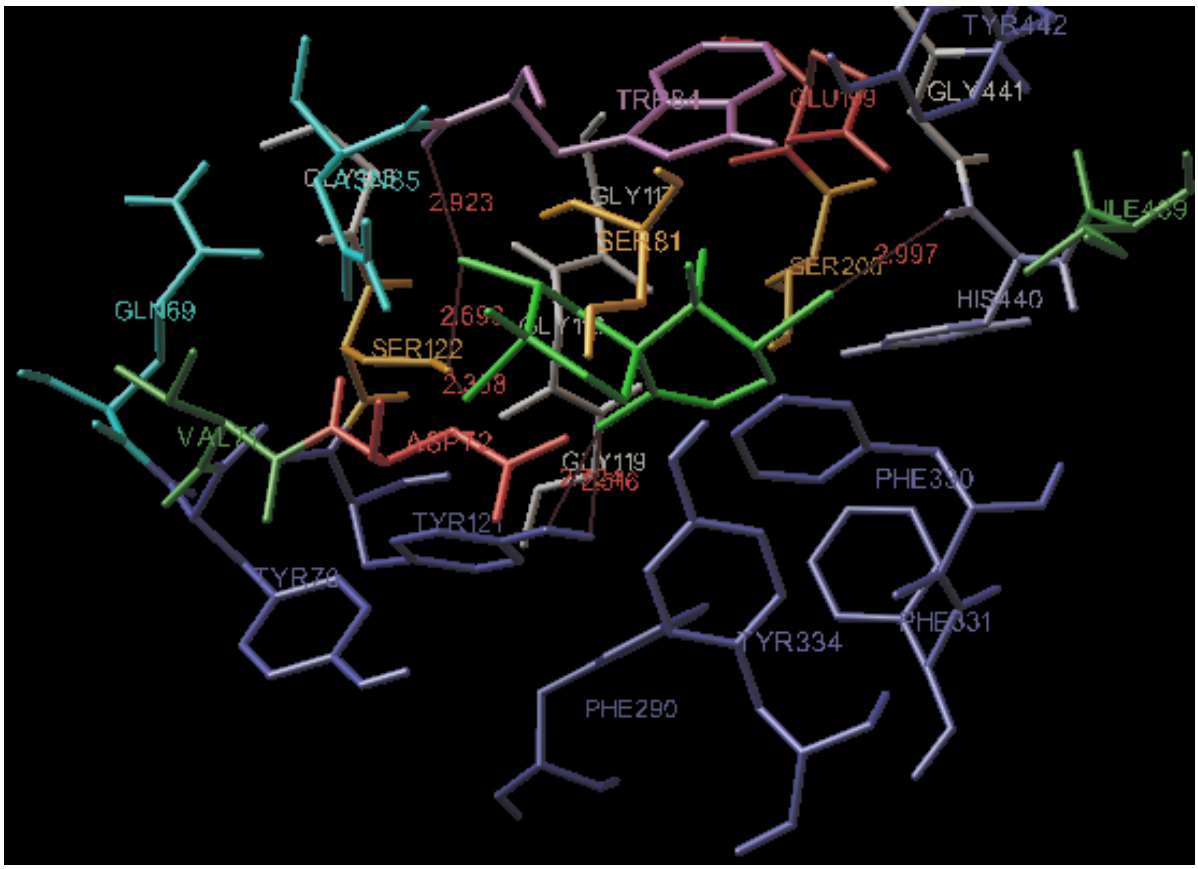
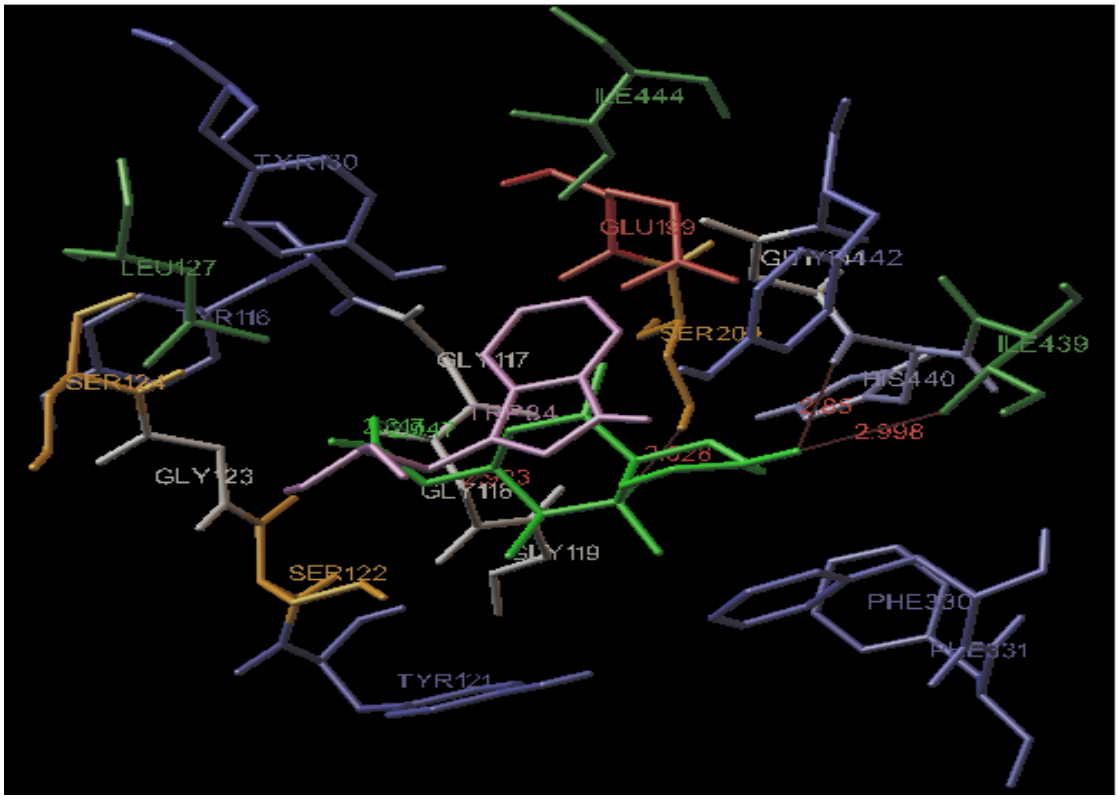


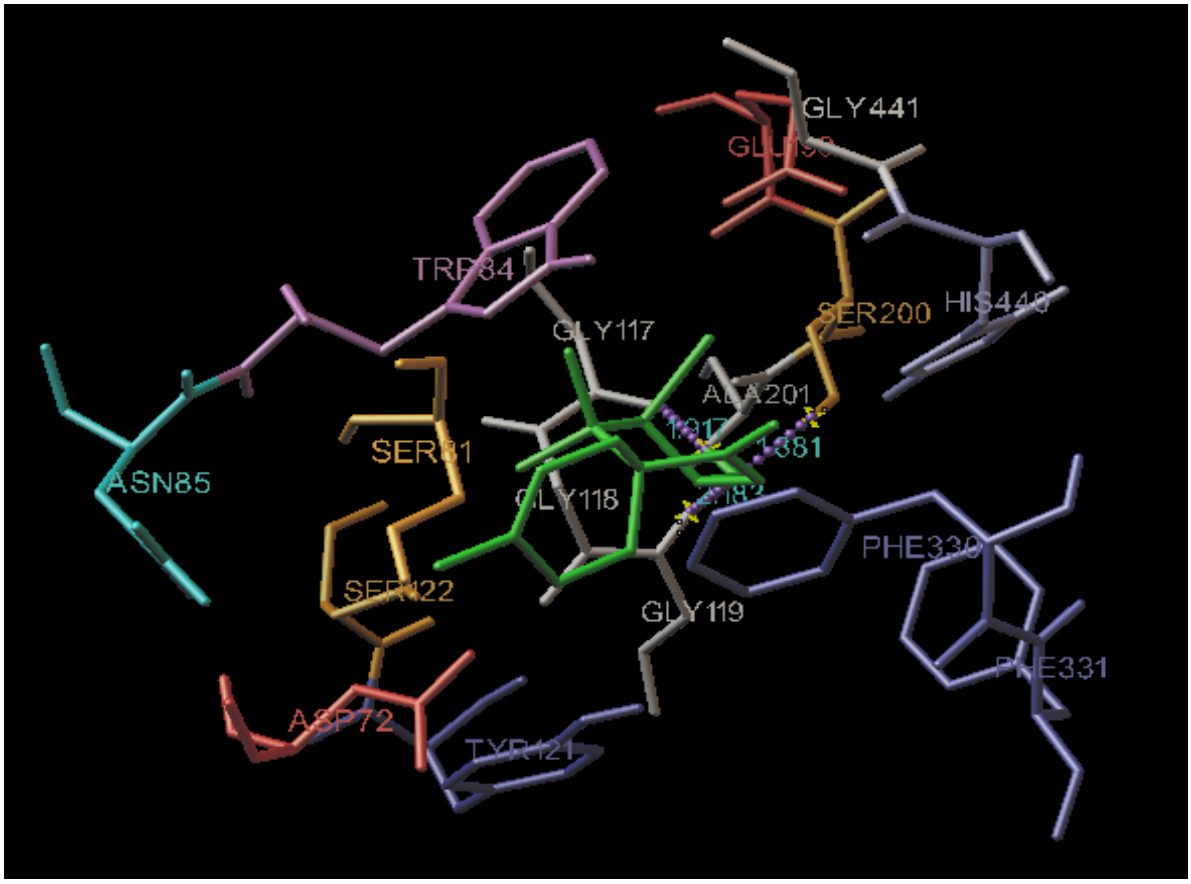
Supplementary Fig. (1). The HOMO-1, HOMO, LUMO and LUMO+1 illustrations (from left to right) of halogenated sesquiterpenes.



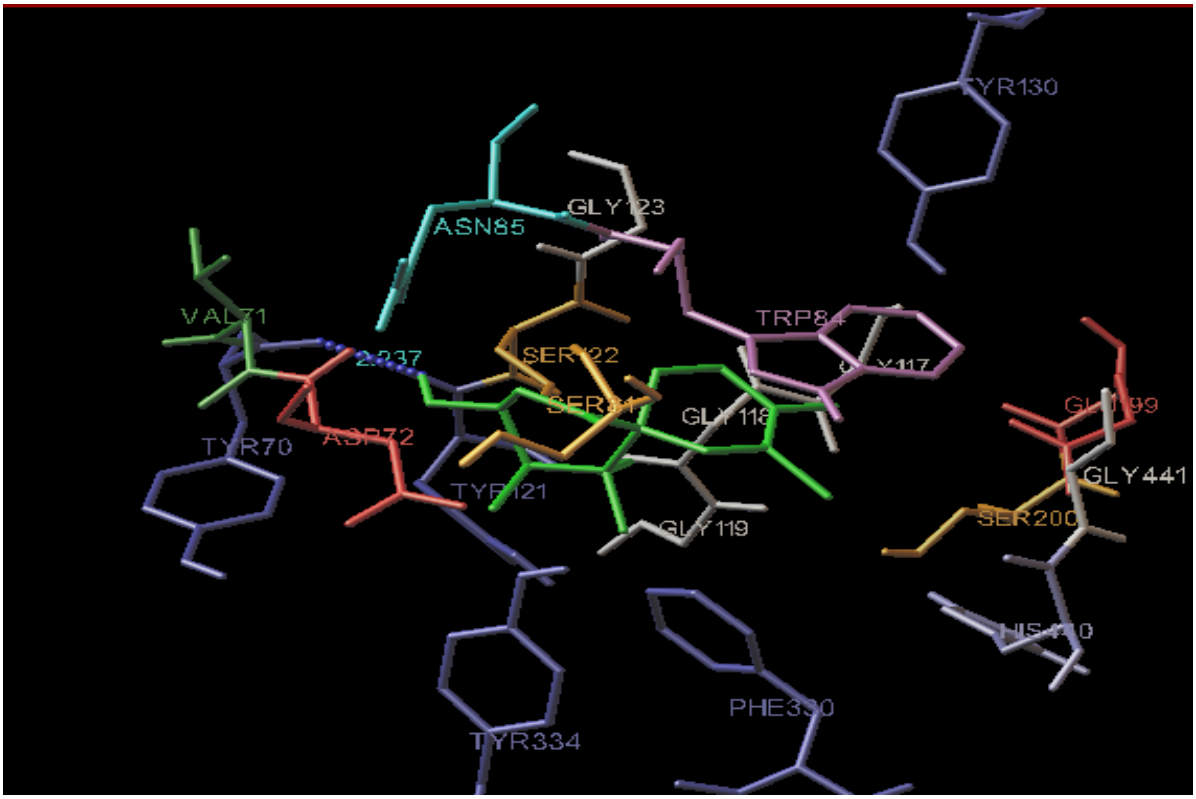
Supplementary Fig. (2). ( ) Molecule **1**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. (The shown distances are in angstrom).



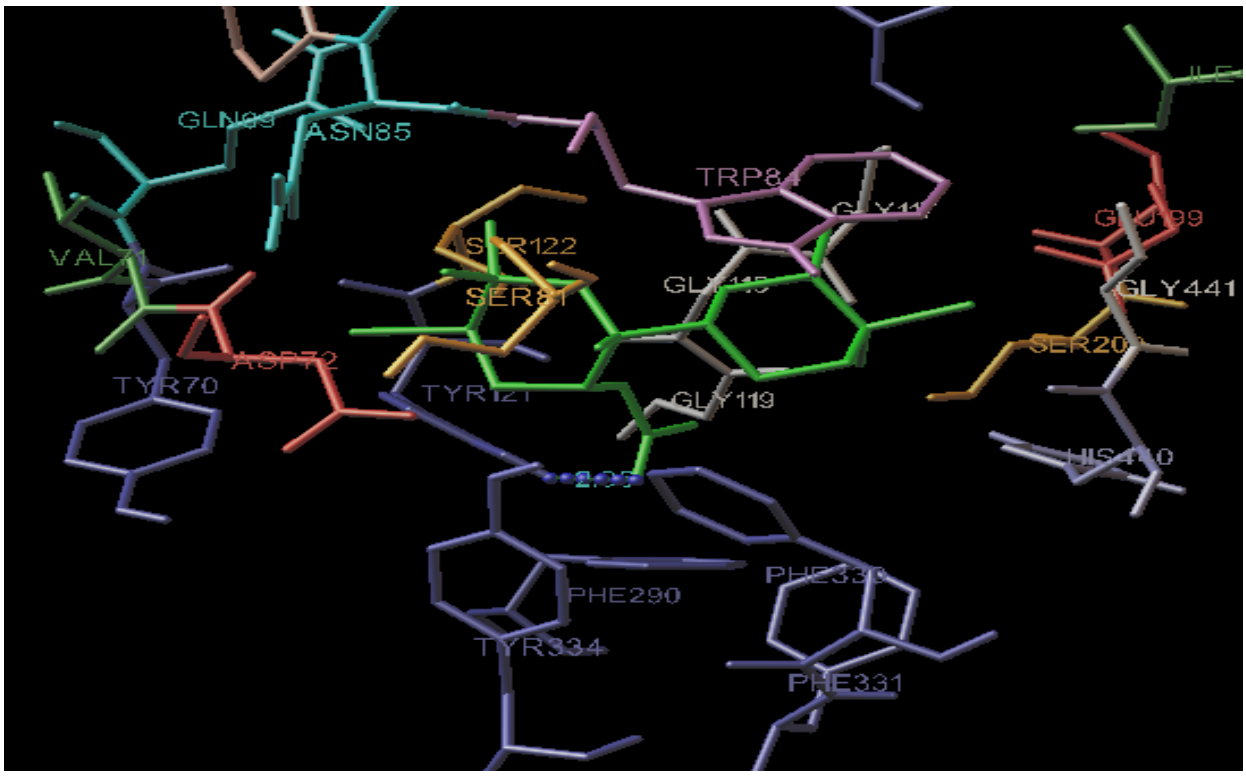
Supplementary Fig. (3). ( ) Molecule **2**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. (The shown distances are in angstrom).



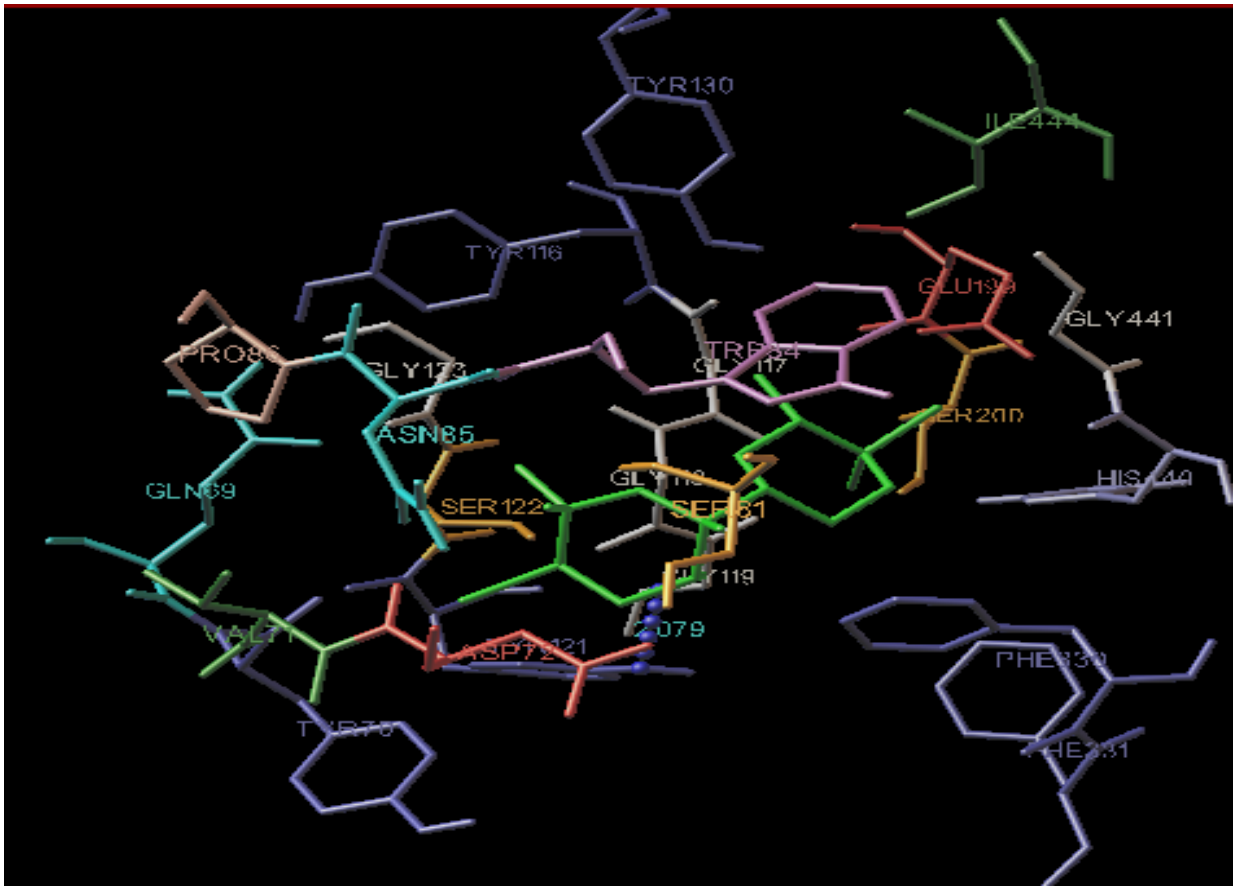
Supplementary Fig. (4). ( ) Molecule **3**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. The purple dots show hydrogen bonds **a**) Gly119 **b**) Ser200 **c**)Gly117. (The shown distances are in angstrom).



Supplementary Fig. (5). ( ) Molecule **5**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. The purple dots show hydrogen bond **a**) Tyr70. (The shown distances are in angstrom).



Supplementary Fig. (6). ( ) Molecule **6**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. The purple dots show hydrogen bonds **a**) Tyr121. (The shown distances are in angstrom).



Supplementary Fig. (7). ( ) Molecule **7**-TcAChE complex showing the inter-molecular interactions with neighbor amino acids. The purple dots show hydrogen bonds **a**) Tyr121. (The shown distances are in angstrom).

Supplementary Table 1. Nearest neighbors and the short intermolecular contact distances (Å) of all the seven molecules in the active site of TcAChE.

Ligand Atom···Amino Acid Residue	Identifier	Distance
1		
C2… Phe330	CE2	3.164
C5… Tyr121	HH	3.283
C8… Trp84	CB	3.239
C11…Phe330	CE2	3.283
Phe330	CZ	3.222
C12…Tyr121	CZ	3.191
Tyr121	OH	2.724
C13…Trp84	CG	3.092
Trp84	CD1	3.101
Trp84	CD2	3.307
C15…Asp72	CB	3.298
Br… His440	O	2.997
Ser122	OG	3.191
Ser122	HG	2.690
Br9…Ser122	OG	3.298
Ser122	HG	2.358
Cl…Trp84	O	2.923
2		
O(Ac) …Gly118	N	2.994
CO…Gly118	HN	2.699
O(Ac)…Gly118	CA	2.984
C3…Gly118	CA	2.923
C7…His440	CD2	2.986
C12…Glu199	OE1	2.922
Phe330	CZ	3.012
C14…Ser200	HG	2.643
C15…His440	O	2.849
3		
OH…Ser200	CB	3.195
Ser200	OG	2.655
Ser200	HG	1.974
Ala201	HN	3.099
Gly117	C	2.879
Gly118	N	3.258
Gly118	CA	2.753
Gly118	C	3.067
Gly119	N	2.611
Gly119	HN	1.820
HO…His440	HE2	3.087
Gly119	N	2.870
C2…Gly118	CA	3.120
C8…Tyr121	OH	3.171
C7…Tyr121	HH	3.179
C13…Ser122	HG	3.123
C14…Trp84	CE3	3.168
C15…Asp72	CB	3.266
Br…Glu199	OE1	3.097
4		
OC…Gln69	OE1	2.986
Trp84	O	3.113
O…Ser122	OG	3.050
CO…Tyr70	O	2.733
CO…Asp72	N	2.883
CO…Asp72	HN	2.149
CO…Asn85	OH1	2.646
C2…Tyr121	OH	2.887
Ser122	HG	2.631
C11…Trp84	CB	3.176
C13…Gly118	CA	3.181
Phe330	CE2	3.016
C14…Tyr121	HH	2.915
C15…Glu199	OE1	3.158
Br…Tyr121	OH	3.093
Cl…His440	O	3.142
5		
OH…Ser122	CB	3.286
Tyr70	C	3.344

Ligand Atom···Amino Acid Residue	Identifier	Distance
HO…Tyr70	O	2.893
Ser122	HG	2.808
Asp72	HN	3.190
C2…Try121	OH	2.781
Tyr121	HH	3.345
C5…Trp84	CB	3.315
C7…Trp84	CB	3.171
C12…Trp84	CB	3.139
C13…Ser122	OG	2.857
C14…Try121	HH	2.796
Phe330	CE2	3.240
Br…Tyr121	OH	3.008
Br…Asp72	CB	2.356
6		
CO…Tyr121	OH	2.702
Phe330	CE2	2.916
Tyr121	OH	2.679
Tyr121	HH	2.065
HO…Tyr121	HH	2.935
Tyr121	OH	3.034
Trp84	CB	3.005
C2…Ser122	HG	2.629
C3…Tyr121	OH	3.143
C5…Phe330	CZ	3.075
C13…Trp84	O	2.724
C14…Asp72	HN	3.244
Asn85	OD1	2.904
C15…Ser200	HG	3.083
His440	CD2	3.236
Cl…Gly441	N	3.310
Glu199	OE1	2.962
Br...Asp72	HN	3.259
Tyr70	O	2.962
Br8…Tyr130	HH	3.288
7		
OH…Tyr121	CZ	2.866
Tyr121	HH	2.201
Ser122	HG	2.818
HO…Tyr121	OH	2.778
Tyr121	HH	2.713
Trp84	CB	3.114
C2…Ser122	HG	2.556
C13…Trp84	O	2.702
C14…Asn85	OD1	2.960
C15…Ser200	HG	2.823
Br…Tyr70	O	2.786
Asp72	HN	2.918
Cl…Glu 199	OE1	2.890
Glu199	OE2	2.935